

REMARKS

I. Status Summary

Claims 8 and 20 are pending in the present application and have been examined.

Claims 8 and 20 were rejected in a Final Official Action dated September 18, 2006 (hereinafter the "Final Official Action") by the United States Patent and Trademark Office (hereinafter "the Patent Office") under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by U.S. Patent No. 5,683,894 to Edwards et al. (hereinafter referred to as "Edwards").

Claims 8 and 20 have been amended. Support for the amendments can be found throughout the specification as filed, including in the Examples and accompanying Figures. Particularly, Examples 3 and 4 discloses *inter alia* the purification of recombinant human proNGF (rh proNGF) from bacterial inclusion bodies, and Figures 2, 4, 6, and 7 demonstrate that the rh proNGF has been purified to at least about 90% purity. Thus, no new matter has been added by the amendments to claims 8 and 20.

New claims 26-28 have been added. Support for the new claims can be found throughout the specification as filed, including particularly in the bridging paragraph between pages 22 and 23 (claim 26) and in the Sequence Listing and on page 13 (claims 27 and 28). Thus, no new matter has been added by the addition of new claims 26-28.

Reconsideration of the application as amended and based on the remarks set forth below is respectfully requested.

II. Summary of the Telephone Interview

A telephone interview was conducted on June 19, 2007 between Examiner Hayes of the Patent Office and applicants' representative Christopher P. Perkins. During the interview, Examiner Hayes discussed the Patent Office's approach to the instant examination of the claims and the perspective with which the cited references have been considered. Additionally, a proposed amendment to claim 8 was discussed. However, agreement was not reached with respect to the allowability of the proposed amended claims.

III. Response to the Rejection under 35 U.S.C. § 102

Claims 8 and 20 stand rejected by the Patent Office upon the contention that these claims are anticipated by Edwards. This rejection has been maintained from prior Official Actions.

After careful consideration of the rejection and the Patent Office's bases therefore, applicants respectfully traverse the rejection and submit the following remarks.

In support of the rejection, the Patent Office asserts that "proNGF isolated from cells is 'substantially purified' from the cell lysate, by definition. Secondly, the term 'substantially purified' is relative term, in which no degree of purification to homogeneity, etc. is alternatively described within the specification nor recited in the claims" (see Final Official Action at page 3).

Applicants respectfully disagree. Initially, applicants respectfully submit that the Patent Office's assertion that proNGF isolated from cells is substantially purified from the cell lysate by definition is an unsupported assertion that fails to comply with the Patent Office's burden under M.P.E.P. § 2144.03. This section states in part:

Official notice without documentary evidence to support an examiner's conclusion is permissible only in some circumstances. While "official notice" may be relied on, these circumstances should be rare when an application is under final rejection or action under 37 CFR 1.113. Official notice unsupported by documentary evidence should only be taken by the examiner where the facts asserted to be well-known, or to be common knowledge in the art are capable of instant and unquestionable demonstration as being well-known. As noted by the court in *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970), the notice of facts beyond the record which may be taken by the examiner must be "capable of such instant and unquestionable demonstration as to defy dispute" (citing *In re Knapp Monarch Co.*, 296 F.2d 230, 132 USPQ 6 (CCPA 1961)).

M.P.E.P. § 2144.03 (emphases added)

Applicants respectfully submit that the instant circumstances do not represent a condition where official notice without documentary evidence to support the Patent Office's conclusion would be proper under M.P.E.P. § 2144.03 and *In re Ahlert*. As the Patent Office has provided no such documentary evidence to support the assertion that

a crude lysate would be understood by one of ordinary skill in the art to be substantially purified with respect to any protein present in the lysate, applicants respectfully submit that the first basis for the instant rejection is improper.

Furthermore, applicants respectfully submit that the Patent Office's assertion is in fact contrary to how one of ordinary skill in the art would understand this term. The Patent Office's attention is directed to the Declaration of Dr. Susan Lorey Pursuant to 37 C.F.R. § 1.132 (hereinafter "the Lorey Declaration") submitted herewith. As set forth in Point 8 of the Lorey Declaration, the method disclosed in Example 4 of Edwards was repeated and lysates that resulted thereby were produced. Although the experiments described in the Lorey Declaration did not include an infection of the mouse L929 cells with a virus, the growth, lysis, clarification, and SDS-PAGE analysis steps were performed precisely as in Edwards.

Exhibit B also submitted herewith shows the results of the Edwards method. Lane 2 shows unequivocally that the clarified extract produced from L929 cells is heavily contaminated with host cell proteins (see *also* point 9 of the Lorey Declaration). Similarly, lane U of **Exhibit C** (submitted herewith, and which corresponds to Figure 2 of the instant application) corresponds to a crude lysate of uninduced bacterial cells that express human pro-NGF, and lane I of **Exhibit C** corresponds to a crude lysate of the same cells after induction of human pro-NGF expression. Applicants respectfully submit that even though the fraction of total protein that corresponds to human pro-NGF in lane I is higher than that in lane U, the extensive host protein contamination in each of these lanes would lead one of ordinary skill in the art to conclude that neither crude lysate is substantially purified for human pro-NGF (see *also* points 10-13 of the Lorey Declaration).

Summarily, applicants respectfully submit that the Patent Office's assertion that one of ordinary skill in the art would consider a protein of interest as being substantially purified when present in a crude lysate has not been supported by any documentation, and thus fails to comply with the Patent Office's burden under M.P.E.P. § 2144.03 and *In re Ahlert*. Furthermore, applicants respectfully submit that they have presented sufficient evidence to demonstrate that the Patent Office's assertion is contrary to the

meaning that one of ordinary skill in the art would attach to the phrase at issue, and thus is improper.

Turning now to the Patent Office's second assertion in support of the instant rejection, the Patent Office asserts that "substantially purified is a relative term, in which no degree of purification to homogeneity, etc. is alternatively described within the specification nor recited in the claims". Applicants respectfully submit that this assertion also fails to support the instant rejection and also represents an improper approach to the examination of this claim terminology. Applicants respectfully submit that a proper framework for reviewing claim terminology for compliance with the second paragraph of 35 U.S.C. § 112 is set forth on M.P.E.P. § 2111, which states in part that "[d]uring patent examination, the pending claims must be 'given their broadest reasonable interpretation consistent with the specification'." Applicants note, however, that M.P.E.P. § 2111 further cites *Phillips v. AWH Corp.* (415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005)) for the proposition that "[t]he Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction 'in light of the specification as it would be interpreted by one of ordinary skill in the art'." *Citing In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004) (emphasis added).

Furthermore, in the absence of a clear definition in the specification to the contrary, "the words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification" (M.P.E.P. § 2111.01, *citing In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); emphasis added). Applicants respectfully submit that the plain meaning of "substantially" is "to a large degree" (as per the online version of the Cambridge Dictionary of American English), and thus a "substantially pure" protein preparation is a preparation in which the protein of interest is purified "to a large degree".

Nonetheless, in an effort to facilitate the instant prosecution, applicants have amended claim 8 to recite *inter alia* that the claimed pharmaceutical preparation comprises purified human proNGF as the active ingredient, wherein the purified human proNGF is purified to at least about 90% purity. Support for this amendment can be

found in throughout the specification as filed, including particularly on page 16, first full paragraph (inclusion bodies "always contained approx. 90-95% rh proNGF (Fig. 2)") and in Figures 2, 4, 6, and 7.

Applicants respectfully submit that Edwards does not disclose a preparation of recombinant human NGF wherein the human proNGF is purified to at least about 90% purity as recited in claim 8. Rather, applicants respectfully submit that at best Edwards discloses a crude cellular lysate that includes murine proNGF.

Accordingly, applicants respectfully submit that claim 8 has been distinguished over Edwards. Claim 20 depends from claim 8, and thus is also believed to be distinguished over Edwards. Accordingly, applicants respectfully request that the rejection of claims 8 and 20 over Edwards be withdrawn at this time.

IV. Discussion of the New Claims

New claims 26-28 have been added. Support for the new claims can be found throughout the specification as filed, including particularly in the bridging paragraph between pages 22 and 23 (claim 26) and in the Sequence Listing and on page 13 (claims 27 and 28). Thus, no new matter has been added by the addition of new claims 26-28.

New claims 26-28 are believed to be distinguished over the Edwards reference cited by the Patent Office for the reasons set forth hereinabove with respect to the rejection of claim 8 under 35 U.S.C. § 102(b). Particularly, applicants respectfully submit that claim 8 has been distinguished over Edwards, and claims 26-28 all depend directly from distinguished claim 8.

Additionally, with respect to claim 26, applicants respectfully submit that Edwards discloses proNGF to have "little to no activity..." in the DRG assay (see Edwards at col. 9, lines 6-9). Applicants respectfully submit that "little to no activity" would not be understood by one of ordinary skill in the art to anticipate or indeed, render obvious, the element "at least about 50% activity... on a molar basis" as recited in claim 26. Therefore, applicants respectfully submit that claim 26 is believed to be patentably distinguished over Edwards on this additional basis.

Accordingly, claims 26-28 are believed to be in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

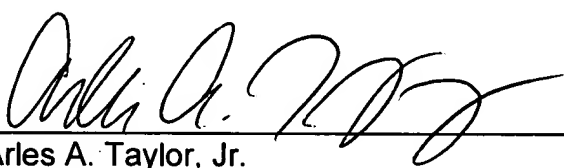
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any underpayment or credit any overpayment of fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: October 11, 2007

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Enclosures: Declaration of Dr. Susan Lorey Pursuant to 37 C.F.R. § 1.132
Exhibits A-E